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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/147,919	03/23/99	CARDOSA	M 2039-705

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EXAMINER	
MOSHER, M	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 03/09/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/147,919	Applicant(s) Cardosa et al
	Examiner Mary Mosh r	Group Art Unit 1648

[X] Responsive to communication(s) filed on *12/11/00*

[ ] This action is **FINAL.**

[ ] Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

[X] Claim(s) *15-31* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

[ ] Claim(s) _____ is/are allowed.

[X] Claim(s) *15-31* is/are rejected.

[ ] Claim(s) _____ is/are objected to.

[ ] Claims _____ are subject to restriction or election requirement.

Application Papers

[ ] See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

[ ] The drawing(s) filed on _____ is/are objected to by the Examiner.

[ ] The proposed drawing correction, filed on _____ is [ ] approved [ ] disapproved.

[ ] The specification is objected to by the Examiner.

[ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

[ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

[ ] All [ ] Some* [X] None of the CERTIFIED copies of the priority documents have been

[ ] received.

[ ] received in Application No. (Series Code/Serial Number) _____ .

[ ] received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

[ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

[X] Notice of References Cited, PTO-892

[ ] Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

[ ] Interview Summary, PTO-413

[ ] Notice of Draftsperson's Patent Drawing Review, PTO-948

[ ] Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1648, Examiner Mosher.

Priority

Applicant argues that the executed four page declaration claimed priority to both the PCT and the DK application. Applicant's attention is directed to page 1 of the declaration, where a "Priority Not Claimed" box is checked for each of the prior applications. However, applicant's response includes a claim to priority, which claim completes the requirements for obtaining benefit of the foreign filing date under 35 U.S.C. 119(a)-(d). Therefore, for the subject matter disclosed in the DK priority document, the effective filing date is now seen as 24 September 1996.

Claim Rejections - 35 USC § 112

Claims 27-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 27 is confusing, because it ends with the word "and". This affects the dependent claims. In the interest of compact prosecution, the final "and" has been ignored. However, this treatment does not relieve applicant of the burden of response to this rejection.

Claims 29-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the

invention, for the same reasons as the previous rejection of claims 9, 10, and 14. Applicant argues that the specification teaches methods of administering the two component composition to an animal and teaches the timing of administration of the two components. However, the teachings are limited to a suggestion to administer parenterally, for example by intramuscular injection. However, this does not address the rejection, which points out that success of the method requires both components to be taken inside the same cells in a manner which produces an effective immune response. Any cell which takes up one component without the other would produce no effect whatsoever. The prior art on T7 promoter/vaccinia combinations is limited to cultured cells which are easily cotransformed or coinfected, simultaneously or sequentially. The prior art does not address whether or not standard methods of vaccine administration, such as IM injection, are capable of delivering two types of molecules so that they co-exist at the same time inside the same cells in vivo. Because of the state of the prior art, one skilled in the art would have reason to doubt an unsupported assertion that conventional methods such as intramuscular injection would supply both plasmid DNA and MVA virus to enough of the same cells, to express enough of the antigen, to produce the desired immune response in vivo. Because of the state of the art, the nature of the invention, the limited teachings in the specification, the lack of any working example, and the absence of any evidence of efficacy of the method as claimed, the rejection is maintained.

Claim Rejections - 35 USC § 103

Claims 15-17, and 19-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Sutter et al (C2) or Altenburger (US 5,185,146), in view of Lai et al (US 5,494,671), and further in view of either Monath et al (Fields Virology) or Kelly et al (US 6,074,865), and any of Moss or Paoletti et al (WO 92/15672) or Nazerian et al (US 5,369,025). In response to the previous rejection, applicant argued that Moss, Bancroft, and Hayes et al did not teach or suggest the use of a recombinant system to express more than one Dengue serotype antigen as a vaccine to provide immunity against all four Dengue serotypes, and that knowledge of antibody-dependent enhancement would have taught away from applicant's invention. In response to this argument, additional references are included in the rejection. Monath et al teaches that, in the Dengue vaccine art since the 1970's, "it was clear that a combination vaccine that simultaneously induced protective immunity against all four serotypes would be required in order to avoid sensitizing the vaccinee to more serious disease (DHF)." See page 1002, column 2. Kelly et al also explicitly suggests a tetravalent vaccine to simultaneously immunize against all four Dengue serotypes, see column 8, lines 1-6 and 38-42. Therefore, those of ordinary skill in the art would indeed have been motivated to vaccinate simultaneously against all four serotypes. If the teachings of Moss are insufficient to provide motivation to use one poxvirus as the vector for antigens of multiple serotypes, Paoletti et al and Nazerian et al teach or suggest examples where a single poxvirus is constructed to express antigens for multiple serotypes of a virus. See Examples 22 and 23 in Paoletti et al (pages 165-176), and in Nazerian et al see the sentence spanning columns 1-2,

and column 2, lines 57-64. Therefore, in view of the combined teachings of the references, it is concluded that there was both motivation and reasonable expectation of success for making a recombinant MVA expressing antigens of all four Dengue serotypes.

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over either Sutter et al (C2) or Altenburger (US 5,185,146), in view of Lai et al (US 5,494,671), and either Monath et al (Fields Virology) or Kelly et al (US 6,074,865), and any of Moss or Paoletti et al (WO 92/15672) or Nazerian et al (US 5,369,025), as applied to claims 15-17 and 19-26 above, and further in view of further in view of Sutter et al (PNAS 89:10847-10851, 1992), for essentially the same reasons as the previous rejection of claim 4. Sutter et al teaches insertion of a foreign sequence at the site of a naturally occurring deletion in MVA, and indicates that MVA has six major deletions totaling 31,000 base pairs. Therefore it would have been obvious to choose one or more of the naturally occurring deletion sites in MVA as a location for inserting one or more foreign DNAs, such as the dengue DNA.

Claims 27-31 are seen as free of the art, because the prior art involving co-expression of multiple products using vaccinia/T7 system uses co-transfection with multiple plasmids (e.g. Zhang et al, BBRC 200:95-101, 1994), and the prior art does not provide particular motivation to co-express multiple Dengue antigens under the control of T7 promoters in a single vector, in a composition with a separate vaccinia virus expressing the T7 promoter. Furthermore, for claims 29-31, the prior art does not provide a reasonable expectation of success for inducing an immune

response in vivo by administration of the two separate components required to express genes in the vaccinia/T7 system, as claimed.

Please note, because WO 92/15672 is a very large patent, only the introductory section and the relevant examples have been provided. Also, in the review by Monath et al, only the section dealing with Dengue virus has been provided.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is (703) 308-2926. The examiner can normally be reached on Monday -Thursday and alternate Fridays from 6:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for this Group is now (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

March 8, 2001

MARY E. MOSHER
PRIMARY EXAMINER
GROUP ~~1800~~ 1600